REMARKS

Status of the Claims

Claims 28-37, 39, and 40 are pending in this application. Claim 40 has been withdrawn from consideration as drawn to a non-elected invention. By this amendment, claims 28, 30, 31, 33, 34, and 35 are amended. Support for these amendments can be found throughout the specification as filed, *inter alia*, at paragraphs [00111] to [00119] and [00190] of the specification as filed. No new matter has been added.

Double Patenting

Claims 28-37 have been rejected on the grounds of nonstatutory obviousness-type double patenting over claims 5-7 of US patent no. 6,670,183. Applicant requests that this rejection be held in abeyance until such time as the present claims have been found to be allowable at which time Applicant will submit a terminal disclaimer.

Claim Rejection Under 35 USC § 112, first paragraph

Claims 28-37, and 39 have been rejected as the Examiner asserts that the specification does not enable those skilled in the art to make and use the presently claimed invention. Applicant requests reconsideration and withdrawal of this rejection in view of the amendments to the claims and the following remarks.

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." MPEP 8th Edition Revision 6 September 2007 at § 2164.04. "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." MPEP 8th Edition Revision 6 September 2007 at § 2164.01 citing *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade

Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). "The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." MPEP 8th Edition Revision 6 September 2007 at § 2164.01 citing *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). "Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." MPEP 8th Edition Revision 6 September 2007 at § 2164.02. "The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." MPEP 8th Edition Revision 6 September 2007 at § 2164.02 citing *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

The Examiner asserts that "while the claims themselves recite that tumor cells and cells expressing PC Cell Derived Growth Factor protein are the cells to be targeted by the antisense oligonucleotides of the invention, the issue is that this recitation does not lend any information towards determining those antisense oligonucleotides which are targeted to PC Cell Derived Growth Factor that carry out the functionality of the instant claims." Final Office Action, page 5.

Independent claims 28, 31, 34, and 35 are drawn to methods that require, *inter alia*, an antisense oligonucleotide that is targeted to at least a portion of SEQ IDNO:16 around the translation initiation site. Independent claim 39 is drawn to a method of inhibiting the expression of PC Cell Derived Growth Factor protein in a cell comprising administering a PC Cell Derived Growth Factor antisense oligonucleotide comprising SEQ ID NO: 14 wherein said oligonucleotide inhibits the expression of PC Cell Derived Growth Factor protein. These claims direct those skilled in the art to specific oligonucleotides that will accomplish the claimed functionality.

The present specification teaches "[i]t is known in the art that sequences around the translation initiation site (ATG encoding the first methionine) provide good sequences for efficient antisense activity." US 2004/0131618 A1 at [0208]. Those skilled in the art would not doubt the objective truth of this statement. The view of those skilled in the art is articulated by Brysch and Schlingensiepen (*Cellular and Molecular Neurobiology* 14(5):557-568, 1994,

reference CJJ on the IDS filed August 14, 2003) as follows: "[t]he most straightforward target region is the start codon and surrounding bases, to interfere with the initiation of protein translation." *Id.* at page 559, citation omitted. Thus, those skilled in the art would objectively believe that antisense oligonucleotides having the characteristics presently claimed would display the claimed functionality.

The Examiner next asserts that the working example provided by Applicant "does not support the full breadth of the claims drawn to a method of inhibition the protein expression of PC Cell Derived Growth Factor in a cell, comprising *any* route of injection of *any* PC Cell Derived Growth Factor antisense oligonucleotide targeted to SEQ ID NO:16." Final Office Action, pages 6-7. The Examiner goes on to state, "one of ordinary skill in the art would have to perform undue experimentation to practice the invention over the scope claimed." Final Office Action, page 7. Applicant respectfully disagrees.

With regard to route of delivery, those skilled in the art understand that delivery of antisense oligonucleotides *in vivo* would not require undue experimentation. For example, Wang et al. state: "[t]hese data quickly led to the conclusion that delivery is not a problem in the application of ODNs [oligonucleotides] *in vivo*." Wang *et al.*, Antisense Nucleic Acid Drug Development 13:169-189, 2000 at page 170, left column. This understanding was shared by those skilled in the art at the time of the invention as evidenced by Mercola *et al.* (*Cancer Gene Therapy* 2:47-95, 1995, reference CGG on the IDS of August 2003) who stated "there is now ample evidence that these compounds [oligonucleotides] do enter the cell, most likely by endocytosis, and they do reach their target." Mercola *et al.* at page 48, left column.

With regard to the particular antisense molecules, it is entirely routine in the art to perform experimentation to identify suitable antisense molecules. For example, Agrawal states "[i]t is considered preferable, therefore, to screen a number of oligonucleotides that encompass different regions on RNA to identify a set of optimal target sites, including the 5'- and 3'-untranslated regions (UTRs), initiation codon site, coding region and intron-exon junctions. Oligonucleotides that have been targeted to the translation initiation codon region of mRNA are generally believed to be more potent than those target to other regions." Agrawal, *Molecular Medicine Today* 6:72-81. 2000 at page 77. Thus, those skilled in the art would consider

screening of oligonucleotides as a routine practice in the art and would objectively believe that the specific oligonucleotides now claimed would have the desired activity.

Given the guidance of the specification, it would not require undue experimentation for one skilled in the art to practice the full scope of the claimed invention without undue experimentation. Applicant respectfully submits that the present specification enables one skilled in the art to make and use the invention as presently claimed and requests withdrawal of this rejection.

Conclusion

In view of the amendments to the claims and above remarks, Applicant believes the pending application is in condition for allowance. Should the Examiner believe the prosecution of the application can be advanced by further discussion of the issues, he is invited to contact Applicant's representative at the telephone number provided below.

Applicant believes no fee beyond those provided for elsewhere in this response is due. However, if an additional fee is due, the Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 22-0185.

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Respectfully submitted,

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